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Coordination Chemistry Reviews
185–186 (1999) 277–295

COORDINATION CHEMISTRY REVIEWS

Heterosupramolecular chemistry: toward the factory of the future

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Received 4 September 1998; received in revised form 9 November 1998

Contents

Abstract

Summarised are the findings of recent studies in which a nanocrystal has been programmed to recognise and selectively bind in solution the following: a molecule, another nanocrystal, or a suitably patterned substrate. These studies form part of an ongoing effort to develop a systematic covalent and non-covalent chemistry of condensed phase and

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PII: S0010-8545(98)00274-4

molecular components. Such a chemistry will under-pin emerging post-information technologies and point the way to the factory of the future.

Keywords: Heterosupramolecular chemistry; Programmed nanocrystal assembly; Post-information technology

1. Introduction

Reviewed are the findings of recent studies directed toward the development of a systematic heterosupramolecular chemistry, i.e. a systematic covalent and non-covalent chemistry of condensed phase and molecular components. In particular, the findings of recent studies directed toward programming a nanocrystal to recognise and selectively bind in solution a molecule, another nanocrystal or a suitably patterned substrate. Having reviewed these findings, their implications for emergent post-information technologies and the factory of the future are considered.

2. Heterosupramolecular chemistry

Conventionally, a supermolecule is distinguished from a large molecule as follows [1]. Firstly, the molecular components of a supermolecule are non-covalently linked; secondly, the intrinsic properties of these molecular components largely persist; and thirdly, the properties of a supermolecule are not a simple superposition of the properties of the constituent molecular components, i.e. there exists a well defined supramolecular function.

With the widespread application of supramolecular concepts throughout chemistry biology and physics, however, has come the need for a more inclusive definition [2]. Consequently, the term supermolecule is now also applied to covalently linked molecular components provided, as above, the properties of these constituent components largely persist and there exists a supramolecular function.

A more inclusive definition still has been adopted in discussing recent work directed toward the development of a systematic chemistry of covalently and non-covalently assembled condensed phase and molecular components [3]. By analogy with a supermolecule, the properties of the constituent condensed phase and molecular components of a *heterosupermolecule* largely persist and there exists an associated *heterosupramolecular* function.

Scheme 1 shows two examples of heterosupermolecules, consisting of a covalently and non-covalently assembled condensed phase (TiO_2 nanocrystal, electron donor) and molecular (viologen, electron acceptor) component [4,5]. In both cases, the associated heterosupramolecular function is light-induced vectorial electron transfer.

Despite the fact that much remains to be done, the growing interest in the covalent and non-covalent assembly of condensed phase and molecular components has resulted rapid progress and growing interest in the emerging area of heterosupramolecular chemistry [4–6].

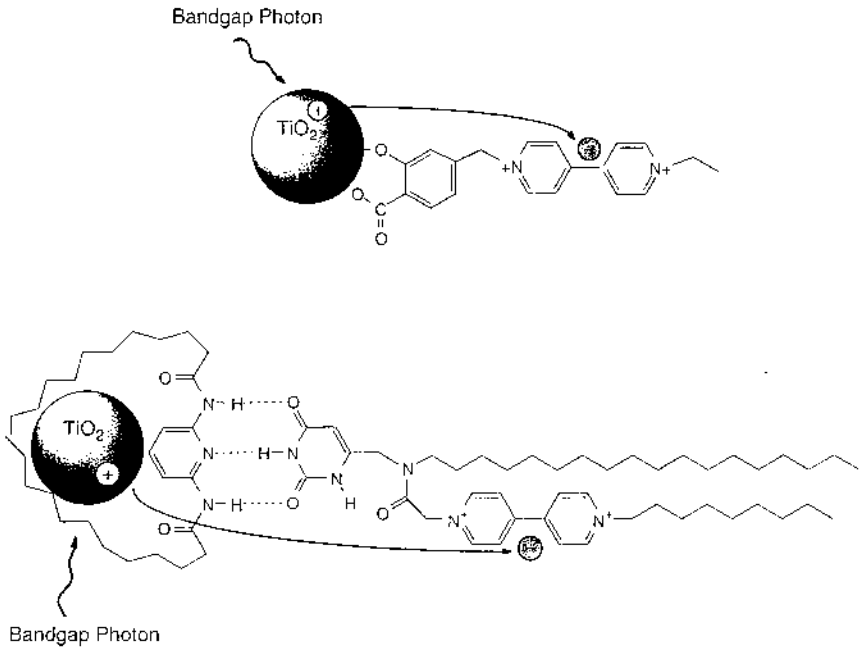
3. Programmed assembly

A consequence of the rapid growth in the area of heterosupramolecular chemistry, is that it is now possible to programme a nanocrystal to recognise and selectively bind in solution the following: a molecule; another nanocrystal; or a suitably patterned substrate. We present an example of how this has been achieved in each case.

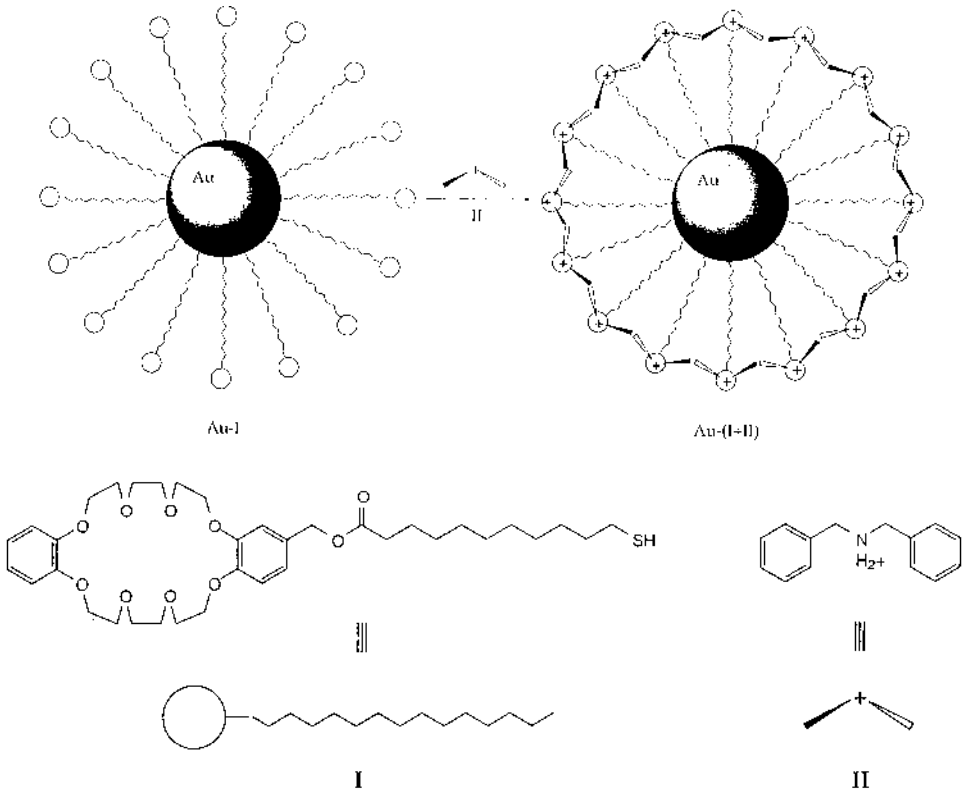
3.1. Programming a nanocrystal to recognise a molecule

A dispersion of Au nanocrystals possessing a narrow size distribution and stabilised by a chemisorbed monolayer of **I**, a dodecane thiol covalently linked to dibenzo[24]crown-8, was prepared. It was expected that these nanocrystals, denoted Au-**I**, would recognise and selectively bind in solution a dibenzylammonium cation, denoted **II**, to form the pseudorotaxane assembly shown in Scheme 2 and denoted Au-(**I** + **II**). Summarised, are findings that showed these expectations to be justified [7].

TEM established that the average diameter of a Au nanocrystal in Au-**I** was 42 ± 8 Å (Fig. 1). Elemental analysis established that the average number of **I**



Scheme 1.



Scheme 2.

adsorbed at the surface of each nanocrystal was 300. On this basis, it was calculated that the average surface area occupied by **I** was 18 $Å^2$. This value was smaller than that for a monolayer of **I** self-assembled at a planar Au substrate (21 $Å^2$) [8], but as might have been expected, somewhat larger than those reported for an alkane thiol adsorbed at the surface of a Au nanocrystal (16 $Å^2$) [9]. These findings were accounted for by the extreme curvature of the Au nanocrystal and the steric hindrance associated with the terminal crown moiety of **I** respectively.

The ^{1}H-NMR spectra (not shown) of **I** and Au-**I** were measured in chloroform-d. In solution, the resonances assigned to the protons α, β and γ to the sulphur moiety in **I** arose at 2.52 ppm (2H, q), 1.61 ppm (2H, m) and 1.36 ppm (2H, m) respectively. However, when **I** was adsorbed at the surface of a Au nanocrystal, these same resonances broadened to such an extent that the α resonance was no longer observed [9]. This contrasted with the observation that the resonances assigned to the protons α, β and γ to the ester moiety in **I** did not broaden significantly. On this basis, it was concluded that all **I** in Au-**I** were adsorbed at the surface of a Au nanocrystal. It was also concluded that, due to the curvature of the Au nanocrystal, the motions of the methylene groups close to the surface of the Au

nanocrystal were constrained, but that this was not the case for methylene groups that extend into the solvent. In short, it was concluded that Au-**I** is accurately represented in Scheme 2.

It had previously been established that the crown ether precursor of **I**, namely dibenzo[24]crown-8, recognises and selectively binds **II** in chloroform-d [10]. It had also been established that a 1:1 pseudorotaxane is formed. It was expected, therefore, that **I** would recognise and selectively bind **II** in chloroform and, also, that a similar 1:1 pseudorotaxane would be formed. To establish whether this was the case, the ^{1}H-NMR spectra (not shown) of **I**, **II** and an equimolar mixture of **I** and **II**, denoted (**I** + **II**), were measured in chloroform-d. The spectral changes observed were similar to those reported for an equimolar mixture of dibenzo[24]crown-8 and **II**, while an analysis of these spectral changes yielded similar values for K_a (2.7×10^4 dm^3 mol^{-1}) and ΔG° (-25 kJ mol^{-1}) [10]. On this

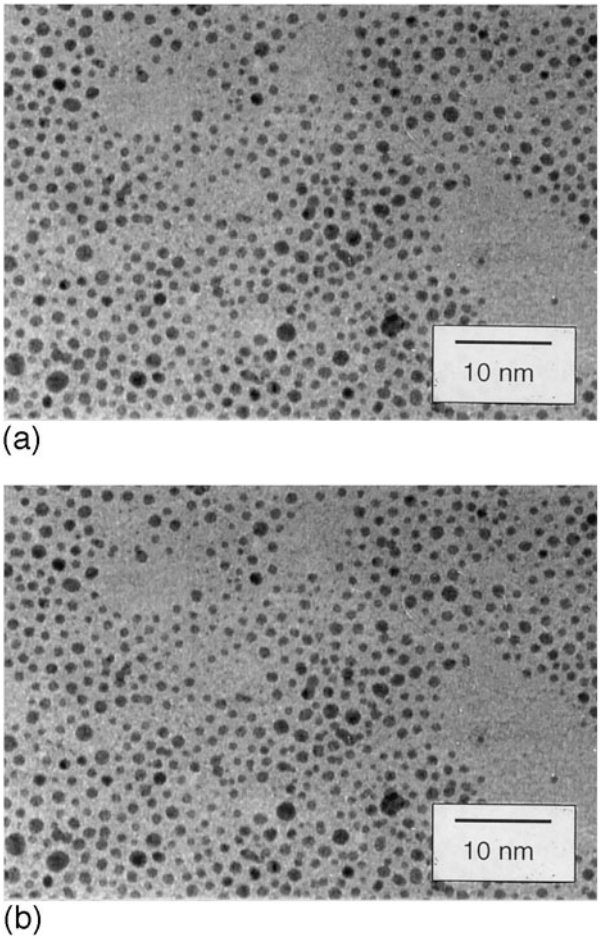


Fig. 1. TEM of Au nanocrystals stabilised by chemisorbed monolayer of (a) **I** and (b) Au-**I**.

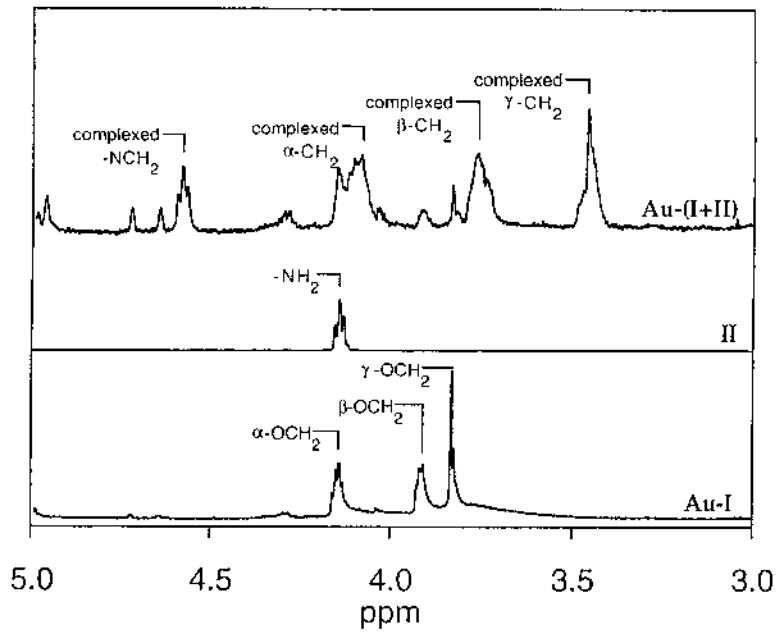


Fig. 2. ^{1}H-NMR spectra of Au nanocrystals stabilised by chemisorbed monolayer of **I**, Au-**I**, **II** and an equimolar mixture of Au-**I** and **II**, Au-(**I** + **II**).

basis, it was concluded that an equimolar mixture of **I** and **II** self-assembles to form a 1:1 pseudorotaxane.

Having established that **I** and **II** form a 1:1 pseudorotaxane in solution, it was expected that Au-**I** would also recognise and selectively bind **II** and form a similar complex. To establish whether or not this was the case, ^{1}H NMR spectra of Au-**I**, **II** and an equimolar mixture of Au-**I** and **II**, Au-(**I** + **II**), were measured in chloroform-d.

In the aliphatic region of Au-**I** (Fig. 2), the resonances assigned to the α, β and γ methyleneoxy protons of the [24]crown-8 ring moiety arose at 4.14 ppm (8H, t), 3.92 ppm (8H, t) and 3.83 ppm (8H, s) respectively. In the same region the resonances assigned to the benzylic protons of **II** arose at 4.15 ppm (4H, t). In Au-(**I** + **II**) the resonances assigned to the α, β and γ methyleneoxy protons of the [24]crown-8 moiety were shifted up-field by 0.05, 0.15 and 0.37 ppm respectively, while the resonances assigned to the benzylic protons of **II** were shifted down-field by 0.43 ppm. These spectral changes were similar to those previously reported for an equimolar mixture of dibenzo[24]crown-8 and **II** [10], and observed for an equimolar mixture of **I** and **II**. On this basis, it was concluded that **I** adsorbed at the surface of an Au nanocrystal in Au-**I** and **II** form a 1:1 pseudorotaxane. In short, that Scheme 2 is an accurate representation of Au-(**I** + **II**).

More quantitatively, an analysis of the spectra in Fig. 2 indicated that 86% of the [24]crown-8 binding sites at the surface of each Au nanocrystal in Au-**I** formed a

1:1 pseudorotaxane with **II**. Not surprisingly, therefore, Au-(**I** + **II**) precipitated from chloroform-d over a period of three hours. It should be noted, however, that these nanocrystals were subsequently re-dispersed by addition of 10% by volume of acetonitrile-d_3 and that this resulted in the percentage of [24]crown-8 binding sites at the surface of each Au nanocrystal that were complexed being reduced to 45%. It should also be noted, that the above re-dispersion was stable for at least three weeks.

As the crown ether binding sites incorporated in **I** were not in solution but were adsorbed at the surface of a Au nanocrystal, a single point determination of K_a based on the nominal concentrations of Au-**I**, **II** and Au-(**I** + **II**) was not appropriate [11]. More appropriate was preparation of a Hill Plot (Fig. 3) with a slope equal to n_H, the Hill Coefficient, and an intercept equal to $-n_H \log(1/K_a)$ (Eq. (1)) [12]. The slope of the Hill Plot yielded a value for n_H equal to 2.21, indicating positive co-operation in the binding process.

$$\log\left(\frac{P_{\text{crown-cation}}}{1-P_{\text{crown-cation}}}\right) = n_H \log[\text{cation}] - n_H \log\left(\frac{1}{K_a}\right) \quad (1)$$

The origin of the above positive co-operativity is not fully understood but is likely due, at least in part, to the following: An increased affinity of **II** for the surface of Au-**I** as the surface of the nanocrystal becomes progressively more polar/hydrophilic. It should be noted, that the above suggestion is consistent with

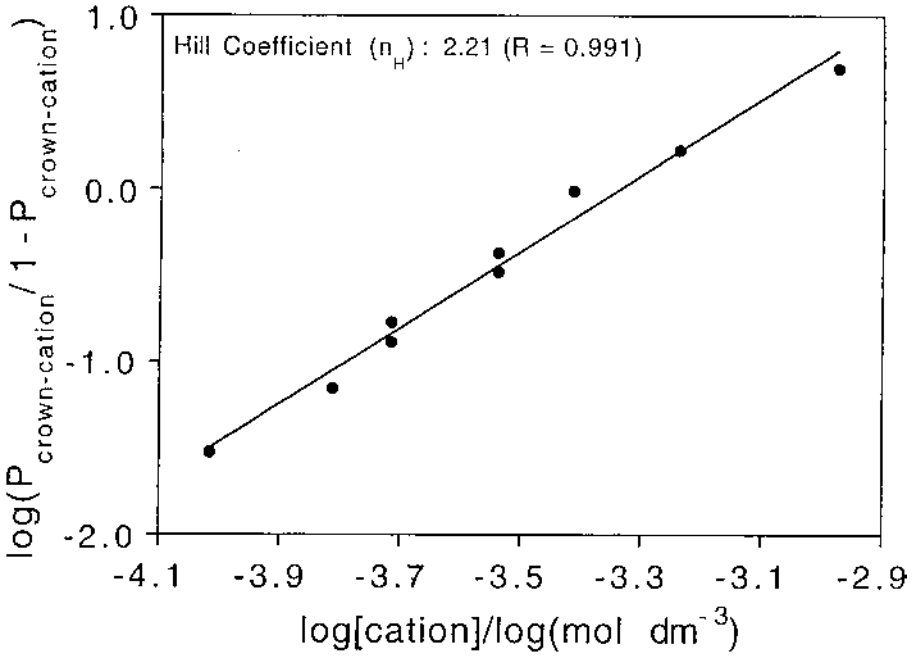
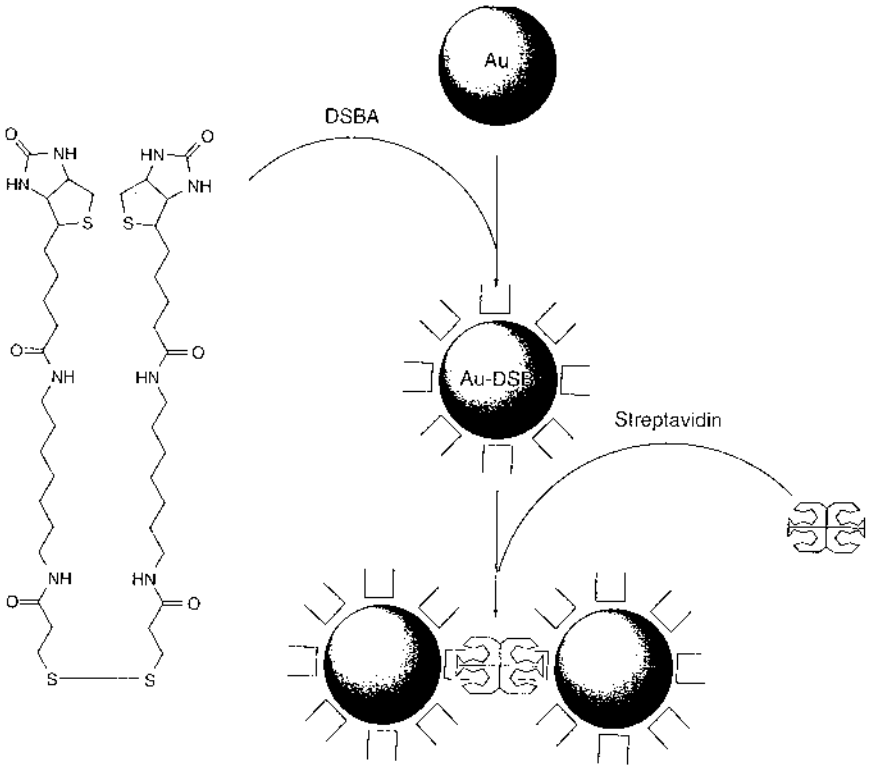


Fig. 3. Hill plot for binding of **II** by Au nanocrystals stabilised by chemisorbed monolayer of **I**, Au-**I**.



Scheme 3.

the observation that Au-(**I** + **II**) precipitated from chloroform-d. Further studies are in progress [13]. It should also be noted, that the above findings also point to similarities between the binding of a molecule in solution by the receptor sites on the surface of a modified nanocrystal and the binding of a drug molecule by the receptor sites on the surface of a cell [11]. These similarities, in turn, raise the intriguing possibility of using such systems as models for cell-drug binding studies and, possibly, as in vivo sensors for such interactions.

3.2. Programming a nanocrystal to recognise a nanocrystal

A charge-stabilised dispersion of Au nanocrystals possessing a narrow size distribution was prepared. These nanocrystals were subsequently modified by chemisorption of the disulphide biotin analogue DSBA. It was expected that addition of streptavidin would enable the biotin modified Au nanocrystals, denoted Au-DSBA, to recognise and selectively bind each other in solution (Scheme 3). Summarised, are the findings of initial studies that showed these expectations to be justified [14].

Au-DSBA aggregation following addition of streptavidin was monitored by dynamic light scattering (DLS) [15]. An increase in the average hydrodynamic radius was observed over time (Fig. 4) [15]. The increase in average hydrodynamic radius was accompanied by a change in the colour of the sol from red to blue. This colour change was attributed to the distance-dependant optical properties of Au nanocrystals [16]. An extensive series of control experiments confirmed that nanocrystal assembly was a consequence of added streptavidin linking bioting modified nanocrytals.

Small angle X-ray scattering (SAXS) was used to probe the structure of the Au-DSBA nanocrystal aggregates in solution. Specifically, the pair-distance distribution function (PDDF) was determined for unmodified Au and Au-DSBA nanocrystals before and after salt and streptavidin induced aggregation respectively (Fig. 5). The PDDF is related to the angular dependence of the intensity of the scattered X-ray radiation by a Fourier transformation (Eq. (2)) [17]:

$$p(r) = \frac{1}{2\pi} \int_0^\infty I(q) qr \sin(qr)\, \mathrm{d}q \tag{2}$$

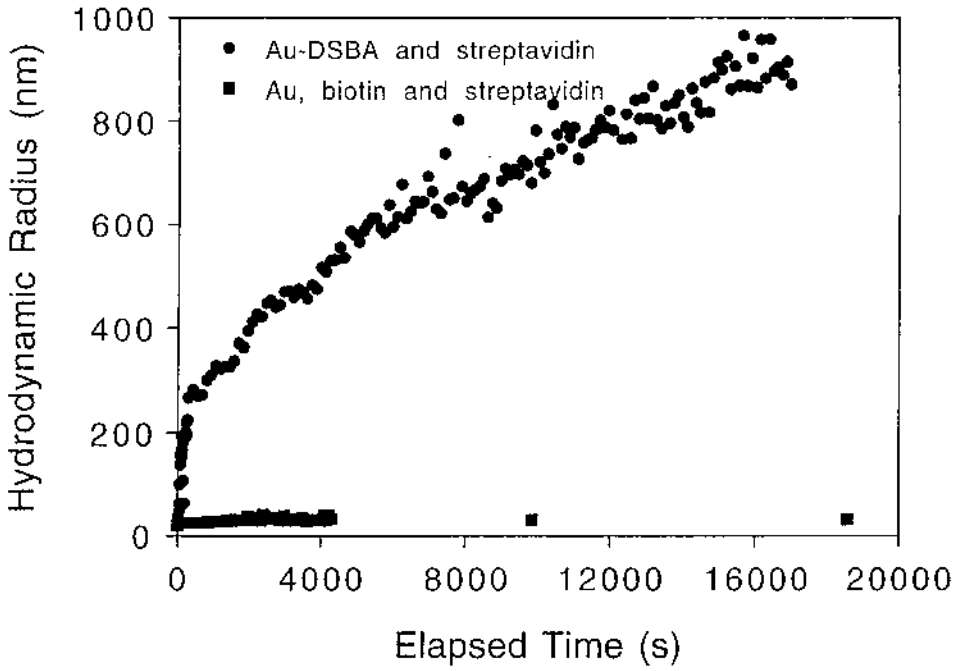


Fig. 4. Hydrodynamic radius against elapsed time for DSBA modified Au nanocrystals, Au-DSBA, following addition of streptavidin and for unmodified Au nanocrystals following addition of free biotin and streptavidin.

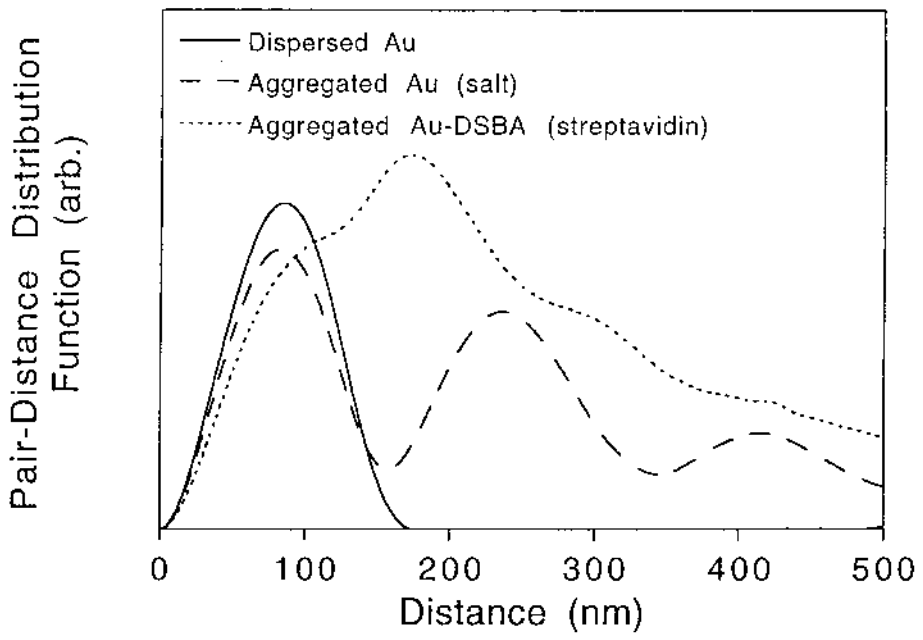


Fig. 5. PDDFs for unmodified Au nanocrystals prior to and following aggregation by addition of a salt and for DSBA modified Au nanocrystals, Au-DSBA, following aggregation by addition of streptavidin.

where $p(r)$ is the PDDF, $I(q)$ is the scattered intensity as a function of the scattering vector, q, which is related to the wavelength of radiation, λ, and the scattering angle, θ, by $q = (4\pi/\lambda)\sin(\theta/2)$. For a dispersion of Au and Au-DSBA nanocrystals prior to aggregation a single maximum in the PDDF was expected and observed. Following salt and streptavidin aggregation of a Au and Au-DSBA nanocrystal dispersion respectively several maxima were expected and observed. In the case of the streptavidin aggregated Au-DSBA nanocrytals, however, the separation between maxima confirmed the presence of the interspersed protein.

Transmission electron microscopy (TEM) was used to image the streptavidin aggregated Au-DSBA nanocrystals. These images revealed the absence of isolated nanocrystals and the presence of aggregates containing, on average, twenty nanocrystals. Furthermore, it was striking that in the above aggregates the constituent nanocrystals were invariably separated by 5 nm, the separation expected if caused by an interspersed streptavidin. In the case of salt aggregated Au nanocrystals, by comparison, isolated nanocrystals and smaller aggregates in which the constituent nanocrystals invariably touched were observed (Fig. 6).

It should be noted that biotin and streptavidin are ideal as a model linking system [18]. This is because the biotin/streptavidin system has one of the largest free energies of association yet observed for the non-covalent binding of a ligand by a protein in aqueous solution ($K_a > 10^{14}$ mol^{-1} dm^3), and because there exists

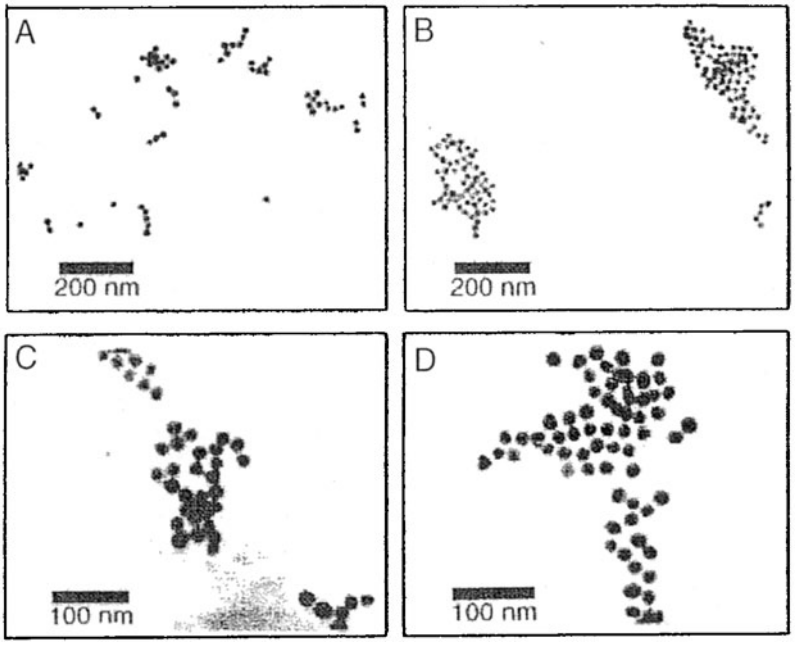
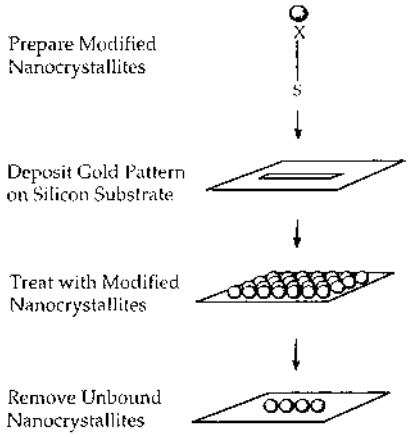


Fig. 6. TEM images of unmodified Au nanocrystals (A and C) and of DSBA modified Au nanocrystals, Au-DSBA, following aggregation by addition of streptavidin (B and D).

a range of readily accessible analogues with K_as in the range 10^0 to 10^{15} mol^{-1} dm^3. It should also be noted, that this is the first example of nanocrystal assembly based on protein binding.



Scheme 4.

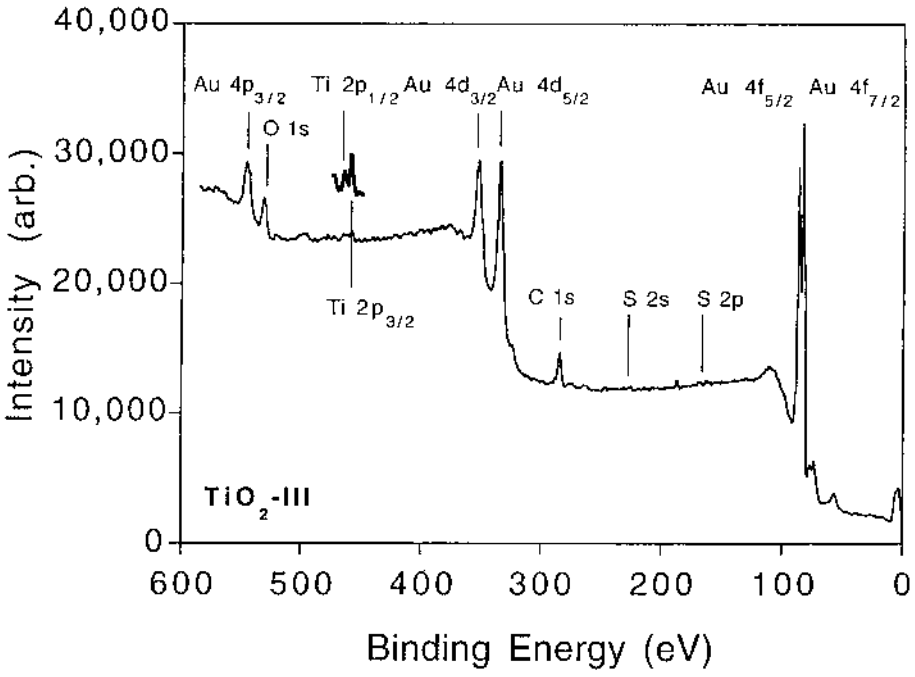


Fig. 7. XPS (K-alpha X-ray emission of Aluminium at 1486.6 eV at a take-off angle of 15°) of a Au patterned silicon wafer substrate modified by adsorbed TiO_2 nanocrystals stabilised by chemisorbed **III**, TiO_2-**III**. Also shown is a higher resolution scan for the same sample between 440 and 490 eV.

3.3. Programming a nanocrystal to recognise a surface

A dispersion of TiO_2 nanocrystals possessing a relatively narrow size distribution was prepared. The nanocrystals in this dispersion were stabilised by chemisorbed decanoic acid incorporating a terminal thiol moiety, **III**. Au patterned silicon wafers were immersed in an ethanolic dispersion of these nanocrystals, denoted TiO_2-**III** (Scheme 4). It was expected that the above nanocrystals would recognise and selectively bind the Au regions on the silicon wafer. Summarised, are the findings of studies that showed these expectations to be largely justified (Scheme 4) [19].

The Au patterned silicon wafers above were initially characterised by X-ray photoelectron spectroscopy (XPS) and reflection-absorption infrared spectroscopy (RAIRS).

The XPS spectrum (Fig. 7) confirmed the presence of Au, S, C, Ti and O [20]. Further, from a higher resolution scan between 440 and 490 eV, peaks at 458 and 464 eV were assigned to the $2p_3$ and $2p_1$ core levels of Ti respectively [20,21]. Based on the above findings, it was concluded that the modified TiO_2 nanocrystals were adsorbed at the patterned Au substrate. The bands assigned to the asymmetric (2926 cm^{-1}, 0.0010 a.u.) and symmetric (2858 cm^{-1}, 0.0005 a.u.) stretches of the

methylene groups in the RAIRS spectrum (Fig. 8) were characteristic of the liquid state. Furthermore, the corresponding absorbances were approximately twice those expected for a monolayer [22].

On this basis, it was concluded that the molecules of **III** adsorbed at the Au patterned silicon wafer were not present as an ordered monolayer but as a disordered bilayer. Further, it was inferred that the TiO_2 nanocrystals adsorbed at the patterned substrate were sandwiched between the adsorbed bilayer (Scheme 5).

To better characterise the patterned Au substrate at which the modified nanocrystals had been adsorbed, high-resolution XPS studies were undertaken at a take-off angle of 45°. Furthermore, since decreasing the take-off angle increases the surface sensitivity of XPS [23], additional high-resolution angle-dependent studies were undertaken at take-off angles of 15, 5, 3 and 1°. The findings of these studies, reported in detail elsewhere [19], are summarised below.

The ratios of the percentage atomic concentrations of Au, S, C, Ti, and O in relevant combinations for a range of take-off angles were determined (Fig. 9). It was expected that for modified TiO_2 nanocrystals adsorbed at a Au patterned silicon wafer substrate the ratio of Ti/Au would increase as the take-off angle deceased. This was observed to be the case. If the modified TiO_2 nanocrystals were adsorbed as shown (Scheme 5), it was predicted that since the functionalised thiols linked to the surface of the nanocrystal may be oriented both into and away from

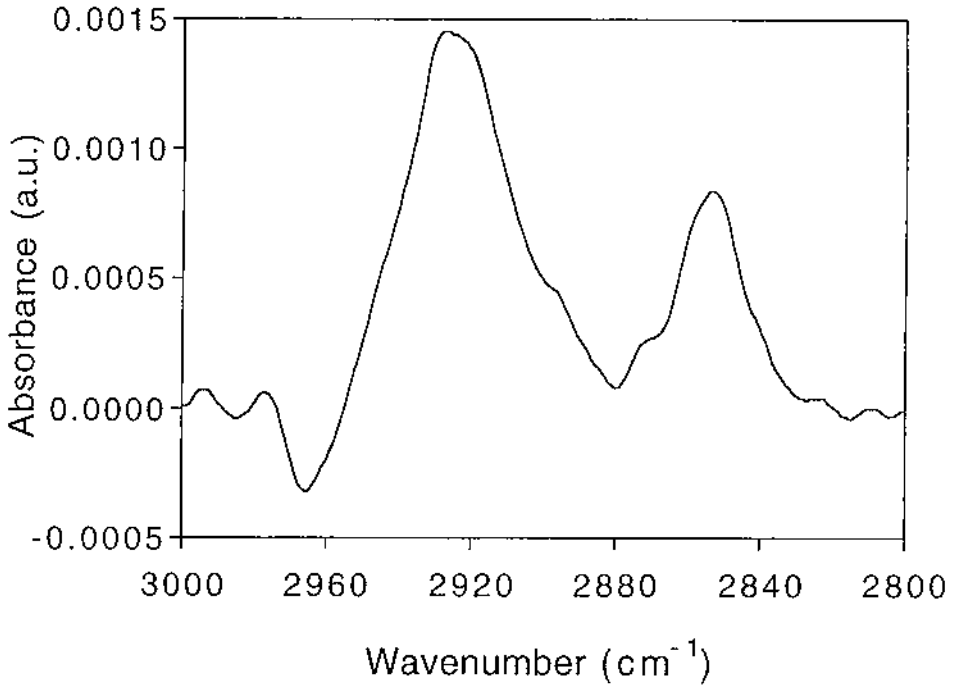
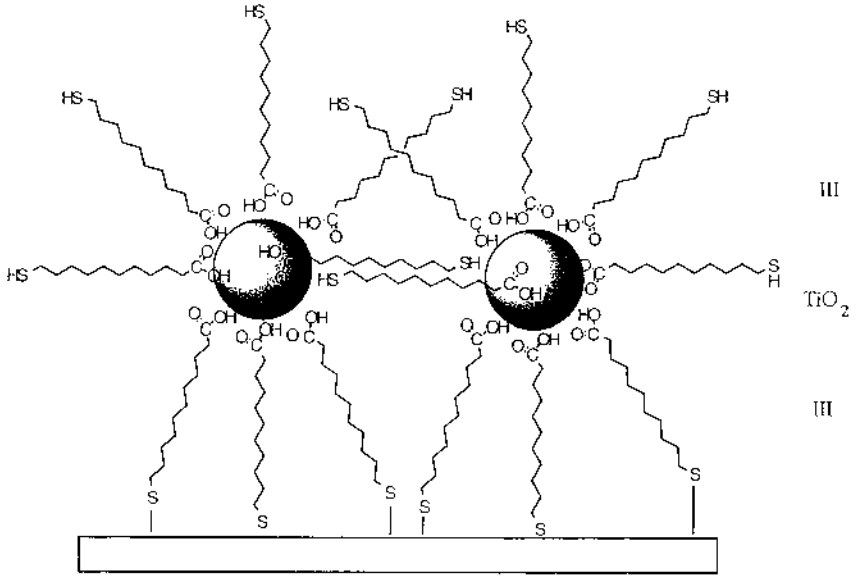


Fig. 8. RAIRS (p-polarised light at an incident angle of 85°) of a Au patterned silicon wafer substrate modified by adsorbed TiO_2 nanocrystals stabilised by chemisorbed **III**, TiO_2-**III**.



Scheme 5.

the Au substrate that the Ti/S ratio would increase and then decrease, i.e. photoelectrons from the S atoms at the Au surface are detected initially while those from the S atoms oriented into the bulk solution are detected subsequently. On this basis, it was also be predicted that while the ratio of Ti/O would be largely independent of the take-off angle, the ratio of S/Au would increase at lower take-off angles. Finally, it was also be predicted that while the ratio of C/O would be largely independent of the take-off angle, the ratio of C/S would initially increase and subsequently decrease at lower take-off angles. All these expectations were met.

The final question to be addressed was the extent of coverage of the patterned Au substrate by the adsorbed TiO_2 nanocrystals. To this end, patterned Au substrates were studied by Rutherford back-scattering (RBS) both prior to and following their immersion in an ethanolic colloid of TiO_2 nanocrystals. Following immersion, the surface coverage of Ti atoms was determined to be 1×10^{15} cm^{-2}. This finding was consistent with a coverage of 0.4 of a monolayer of 20 Å diameter TiO_2 nanocrystals. It was noted that because the TiO_2 nanocrystals adsorbed at the patterned Au substrate were modified by adsorbed **III**, their distance of closest approach is limited and coverage will be less than a monolayer. A TEM image of this substrate showed the presence of about 0.4 of a monolayer of adsorbed TiO_2 nanocrystals whose diameters ranged from 20 to 30 Å (Fig. 10).

For all of the experimental techniques described above (XPS, RIARS, RBS and TEM) appropriate control experiments were performed using silicon substrates [19].

It was concluded that no irreversible adsorption resulted, that is adsorption that was not easily reversed by washing.

Our current work is directed toward programming nanocrystals, or their assembles, to recognise and selectively bind patterned substrates using the approach outlined above [24]. Adopting this approach, it is hoped it will prove possible to self-assemble, from solution, complex nanocrystal assemblies at a substrate. It is noted that similar findings and objectives have been reported by other workers [25].

4. Factory of the future

As may be seen from the findings reviewed in the previous section, it has proved possible to programme a nanocrystal to recognise and selectively bind a molecule, a nanocrystal or a suitably patterned substrate. The implications of these findings for the development of post-information technologies and the factory of the future are considered below.

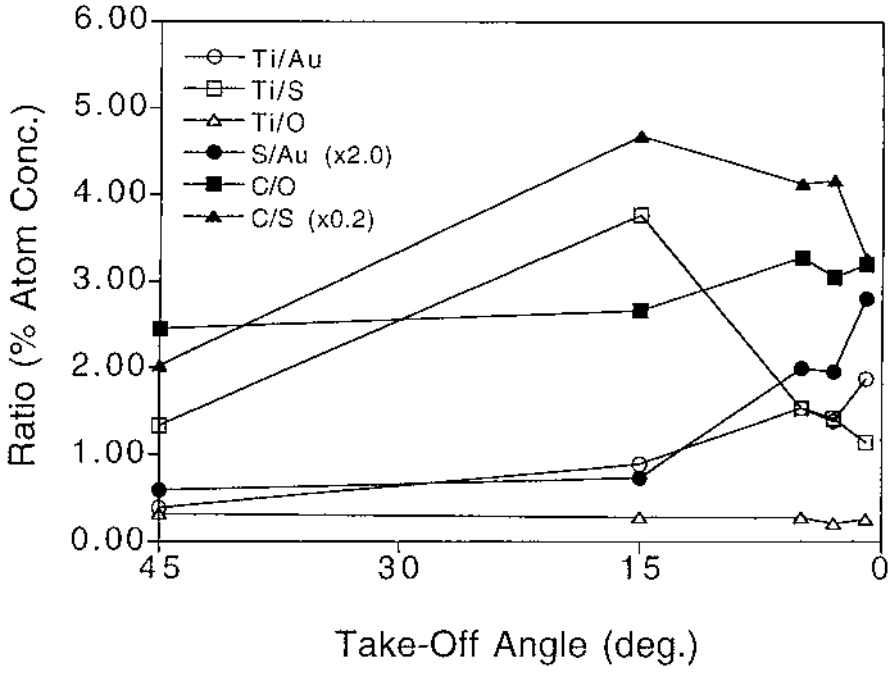


Fig. 9. Take-off angle dependence of the ratios of the percentage atomic concentration of the indicated elements as determined by XPS (K-alpha X-ray emission of Aluminium at 1486.6 eV) for a Au patterned silicon wafer substrate modified by adsorbed TiO_2 nanocrystals stabilised by chemisorbed **III**, TiO_2-**III**.

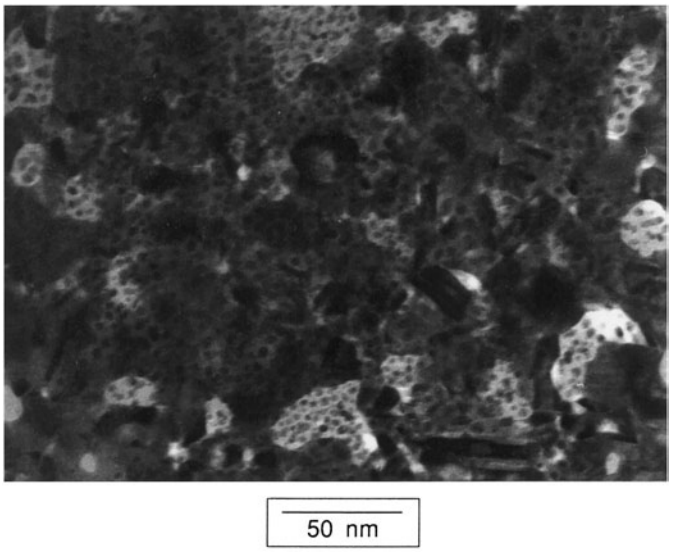


Fig. 10. TEM of a Au patterned silicon wafer substrate modified by adsorbed TiO_2 nanocrystals stabilised by chemisorbed **III**, TiO_2-**III**.

4.1. Post-information technologies

Future growth of the information technology (IT) sector will depend on developing faster integrated circuits (ICs) and on reducing costs. In this context, the major organisations in the sector predict that incremental improvements in existing lithographic technologies will lead to the cost-effective manufacture of ICs based on 50 nm heterostructures. These organisations also predict that this milestone will be met by 2020. Thereafter, however, further increases in speed and reductions in cost will be predicated on an understanding of how to design and operate ICs based on heterostructures whose properties are strongly size dependent and on the development of a practical non-lithographic manufacturing technology. Satisfying these prerequisites are the two principle objectives of the emerging post-information technologies.

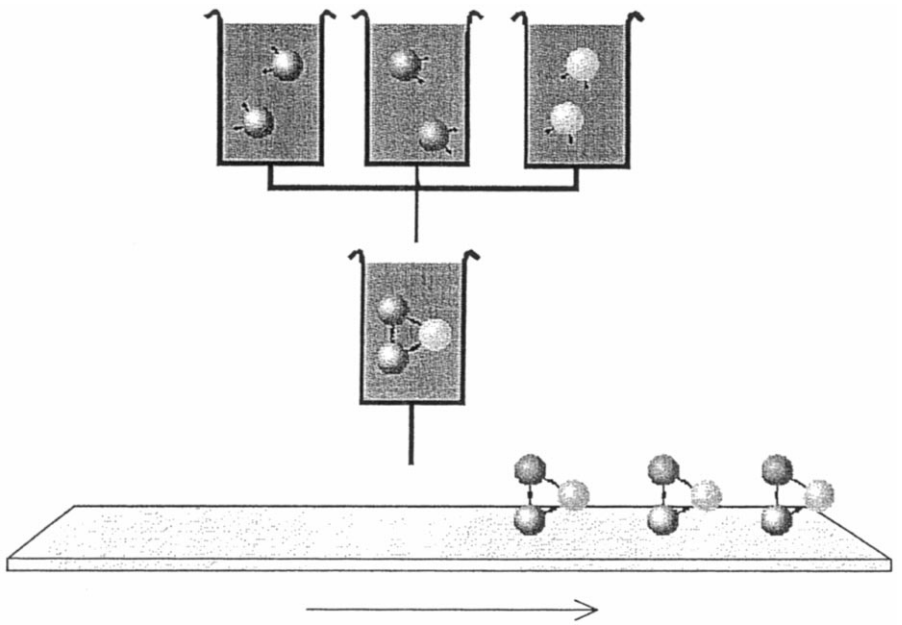
In respect of both of these objectives, the assembly in solution or at a suitable substrate of complex metal, semiconductor and insulator nanocrystal architectures is of particular interest [1–14]. In the medium term, it is expected such studies will lead to the assembly of arrays of functional nanoscale heterostructures whose study will provide insights into the design and operation of ICs based on heterostructures whose dimensions are of the order of a few tens of nanometers. In the longer term, it is possible such studies will lead to the cost-effective assembly (partial or complete) in solution or at a suitable substrate of ICs capable of processing information at unprecedented speeds. If, however, these expectations are to be realised it will be necessary to develop practical strategies for the assembly of complex nanocrystal architectures in solution or at a suitable substrate.

One strategy, is to adsorb molecules incorporating a binding site at the surface of each nanocrystal of a dispersion (Scheme 6). The function of these molecules is to uniquely define the position of a nanocrystal from a given dispersion within the nanocrystal architecture to be assembled. Upon mixing a number of such dispersions, each nanocrystal will recognise and selectively bind a nanocrystal from another dispersion or a well-defined region on a patterned substrate. By this means, it will be possible to programme the parallel assembly of identical multiple copies of the desired nanocrystal architecture in solution or at a suitable substrate. These and related strategies my well give rise to the factory of the future.

Clearly, underpinning the above strategy are efforts directed toward development of a systematic chemistry of both condensed phase and molecular components [15–17]. Equally clearly, while much remains to be done, the findings reviewed above are encouraging and justify further investigation.

4.2. A coming together of the materials and life sciences

The strategy outlined above, where the constituent heterostructures of ICs are assembled from programmed nanocrystals in solution can, in principle, be extended to the assembly of any structure. That is, provided the necessary molecular and condensed phase components are available and provided they can be sufficiently well programmed. While it is the forte of molecular and materials chemists to prepare and characterise condensed phase and molecular components with any



Scheme 6.

desired property, it is the forte of nature to assemble condensed phase and molecular components into highly complex architectures, even to the point of endowing the resulting assembly with the capacities for self-repair and self-replication. For this reason, the emerging post-information technologies and the manufacturing technologies of the future will owe as much to the life sciences as to the materials sciences.

Acknowledgements

The work reviewed here was funded by the Commission of the European Communities as part of the Non-Nuclear Energy Programme (Contract JOR3-CT96-0107) and the Training and Mobility of Researchers (Network) Programme (Contract FMRX CT96-0076).

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